



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 3220-60980		FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US98/18416	International filing date (day/month/year) 03/09/1998	Priority date (day/month/year) 05/09/1997	
International Patent Classification (IPC) or national classification and IPC C12N15/82			
Applicant PURDUE RESEARCH FOUNDATION et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application 			
Date of submission of the demand 12/03/1999		Date of completion of this report 29. 11. 99	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Claes, B Telephone No. +49 89 2399 3429 	

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US98/18416

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*:

Description, pages:

1-31 as originally filed

Claims, No.:

1-19 as originally filed

Drawings, sheets:

1/5-5/5 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 9.

because:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US98/18416

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 9 are so unclear that no meaningful opinion could be formed (*specify*):
- see separate sheet**
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2.5-7,12,13
	No:	Claims	1.3,4,8,10,11,14
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-8,10-19
Industrial applicability (IA)	Yes:	Claims	1-8,10-19
	No:	Claims	

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US98/18416

Re Item I

Basis of the opinion

The application contains a sequence listing pages 1-2.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 9: In paragraph 2 of claim 9 there is no particular definition of the structural gene contained in the construct, whereas paragraph 3 appears to suggest this gene to be of a particular nature or function (encoding said biologically detrimental compound). This internal inconsistency does not allow proper examination of the claim.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The following documents are referred to:

D1 = Kilby et al. (1995), The Plant J., 8(5), p.637-652.

D2 = Lloyd & Davis (1994), Mol. Gen. Genet., 242, p.653-657.

D3 = Lyznik et al. (1993), NAR, 21(4), p.969-975.

D4 = Lyznik et al. (1995), The Plant J., 8(2), p.177-186.

D5 = US-5,658,772

D6 = WO96/04393

D7 = WO97/13401

2. D1 (see abstract, Fig.2), D2 (see Fig.1), D3 (see Fig. 2), D4 (Fig.3) and D5 (column 22 lines all disclose plant expression vectors comprising a promoter, a blocking sequence and a structural gene, in which the blocking sequence is flanked by direct FRT repeats and in which the structural gene becomes operably linked to the promoter after removal of the blocking sequence. Hence, these documents are prejudicial for the novelty of claims 1 and 8 (Article 33(2) PCT objection).

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US98/18416

The disclosures in D1 and D4 are furthermore prejudicial for the subject matter of claims 3 and 4 (Article 33(2) PCT objection).

3. D5 discloses the use of the Lox/Cre system in similar applications as the present application discloses for the FLP/FRT system. D5 discloses various constructs and crossing schemes. The crossing scheme of claim 10 is disclosed in D5 in e.g. columns 28-31 and 40-42. This disclosure is novelty destroying for the subject matter of claim 10, 11 and 14 (Article 33(2) PCT objection and renders the subject matter of claim 12 in view of the statements in column 5 lines 39-42 (Article 33(3) PCT objection).

D6 discloses, inter alia, a system in which a "transient promoter is linked via a blocking sequence, which includes a male sterility gene (see e.g. p.10 line 17 - p.11 line 16, p.14 lines 28-31, p. 16 lines 7-18), and which is surrounded by "excision sequences" to a structural gene. A plant comprising such a construct is crossed with a plant expressing a recombinase specific for the "excision sequences".

This disclosure is novelty destroying for the subject matter of claim 10, 11 and 14.

D2 (see Table 1) discloses the method as subject matter of claims 10 and 13 (Article 33(3) PCT objection).

4. D6 further discloses the structural gene the expression of which is to be restored to be a suicide gene or a gene that encodes a product that disrupts normal cell function (see p.9 lines 8-18). The difference between this disclosure and the subject matter of claim 2 is the fact that in stead of the Lox/Cre system the FLP/FRT system is used.

From D1-D4, however, the skilled person can take that the FLP/FRT system is as efficient as the Lox/Cre excision system in plants.

Therefore, the skilled person would routinely replace the "excision system" as applied in D6 by the system as described in either of D1-D4 and arrive without any undue burden at the subject matter of claim 2 (Article 33(3) PCT objection).

**INTERNATIONAL PRELIMINARY
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International application No. PCT/US98/18416

An analogous objection applies against the subject matter of claim 13.

5. Furthermore, in view of the indicated interchangeability of the structural genes of interest indicated in D6 or D1-D4, the construction of appropriate polylinker containing cloning constructs cannot be based on inventive skill. Hence, the subject matter of claims 5-7 cannot be accepted to involve an inventive step.
6. None of the cited documents appear to disclose a system as described in claim 15, i.e. in which the male sterile maintainer line has as a blocking sequence comprising a suicide gene operable linked to a "seed specific promoter" (as opposed to e.g. a pollen or tapetum specific promoter in D6 or D7).

Although it is at present unclear what the advantage of such a construct set up could be, in view of the fact that the such method appears not to have been rendered obvious by the prior art, claims 15-19 relate to novel and inventive subject matter.

09/11/99 904

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PATENT COOPERATION TREATY

HS 131a

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

LAMMERT, Steven
BARNES & THORNBURG
11 South Meridian Street
Indianapolis, IN 46204
ETATS-UNIS D'AMERIQUE

RECEIVED

DEC 08 1999

BARNES & THORNBURG

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing
(day/month/year)

29. 11. 99

Applicant's or agent's file reference
3220-60980

IMPORTANT NOTIFICATION

International application No.
PCT/US98/18416International filing date (day/month/year)
03/09/1998Priority date (day/month/year)
05/09/1997

Applicant

PURDUE RESEARCH FOUNDATION et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



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D-80298 Munich
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Authorized officer

Vullo, C

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 3220-60980	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 98/ 18416	International filing date (day/month/year) 03/09/1998	(Earliest) Priority Date (day/month/year) 05/09/1997
Applicant PURDUE RESEARCH FOUNDATION et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (see Box I).
2. ☐ Unity of invention is lacking (see Box II).
3. ☒ The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing

☒ filed with the international application.
☐ furnished by the applicant separately from the international application.

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority
4. With regard to the **title**, ☒ the text is approved as submitted by the applicant
☐ the text has been established by this Authority to read as follows:
5. With regard to the **abstract**, ☒ the text is approved as submitted by the applicant
☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.
6. The figure of the **drawings** to be published with the abstract is:
 Figure No. 1a ☒ as suggested by the applicant. ☐ None of the figures.
☐ because the applicant failed to suggest a figure.
☐ because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/18416

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/82 A01H5/00 A01H5/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N A01H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KILBY N. ET AL.: "FLP recombinase in transgenic plants: constitutive activity in stably transformed tobacco and generation of marked cell clones in Arabidopsis" PLANT JOURNAL, vol. 8, no. 5, 1995, pages 637-652, XP002089983 see the whole document	1,3,4,8
X	LLOYD A M ET AL: "FUNCTIONAL EXPRESSION OF THE YEAST FLP/FRT SITE-SPECIFIC RECOMBINATION SYSTEM IN NICOTIANA TABACUM" MOLECULAR AND GENERAL GENETICS, vol. 242, 1994, pages 653-657, XP002043804 see the whole document	1,3, 8-10,13, 14

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

14 January 1999

Date of mailing of the international search report

29/01/1999

Name and mailing address of the ISA

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NL - 2280 HV Rijswijk
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Authorized officer

Kania, T

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/18416

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 658 772 A (ODELL JOAN TELLEFSEN ET AL) 19 August 1997 see esp. pp. 9-14 ---	9-11, 14
X	WO 96 04393 A (US GOVERNMENT ; DELTA & PINE LAND CO (US)) 15 February 1996 see the whole document, esp. pp. 5-18 ---	1-3, 8-11, 13-16, 18
A	WO 97 13401 A (LEE JANG YONG ; HODGES THOMAS K (US); HUQ ENAMUL (US); LYZNIK LESZE) 17 April 1997 see the whole document ---	1-19
A	LYZNIK L A ET AL: "Activity of yeast FLP recombina- se in maize and rice protoplasts." NUCLEIC ACIDS RESEARCH, (1993 FEB 25) 21 (4) 969-75. JOURNAL CODE: 08L. ISSN: 0305-1048., XP002089984 ENGLAND: United Kingdom see the whole document ---	1-19
A	LYZNIK L A ET AL: "Heat-inducible expression of FLP gene in maize cells." PLANT JOURNAL, (1995 AUG) 8 (2) 177-86. JOURNAL CODE: BRU. ISSN: 0960-7412.. XP002089985 ENGLAND: United Kingdom see the whole document -----	1-19

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 98/18416

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5658772 A	19-08-1997	AU 639059 B	15-07-1993
		AU 6974791 A	24-07-1991
		CA 2071943 A	23-06-1991
		EP 0506763 A	07-10-1992
		IL 96768 A	10-06-1997
		WO 9109957 A	11-07-1991
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WO 9604393 ✓ A	15-02-1996	US 5723765 A	03-03-1998
		AU 696668 B	17-09-1998
		AU 3205095 A	04-03-1996
		BR 9508471 A	28-10-1997
		CA 2196410 A	15-02-1996
		EP 0775212 A	28-05-1997
		JP 10503377 T	31-03-1998
		ZA 9506410 A	11-03-1996
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WO 9713401 ✓ A	17-04-1997	AU 7662896 A	30-04-1997
		CA 2234557 A	17-04-1997
		EP 0876094 A	11-11-1998
		US 5677175 A	14-10-1997
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INTERNATIONAL COOPERATION TREATY

FOR Search/A19BY led

From the INTERNATIONAL SEARCHING AUTHORITY

NO 51899 PCT

To:

BARNES & THORNBURG
Attn. LAMMERT, S.
11 South Meridian Street
Indianapolis, IN 46204
UNITED STATES OF AMERICA

FEB 05 1999

BARNES & THORNBURG

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing
(day/month/year)

29/01/1999

Applicant's or agent's file reference

3220-60980

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/US 98/18416

International filing date

(day/month/year)

03/09/1998

Applicant

PURDUE RESEARCH FOUNDATION et al.

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicants's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

With **30 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



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Nancy Gamme